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ILLUMINATING THE PATH TO BETTER HEALTH
Colon Cancer

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Definition

• Colon cancer is cancer of the large intestine (colon), the lower part of your digestive system. Rectal cancer is cancer of the last several inches of the colon. Together, they're often referred to as colorectal cancers.
Definition

- Most cases of colon cancer begins as small, noncancerous (benign) clumps of cells called adenomatous polyps. Over time some of these polyps become colon cancers.
Most colorectal cancers develop slowly over several years. Before a cancer develops, a growth of tissue or tumor usually begins as a non-cancerous polyp on the inner lining of the colon or rectum. A tumor is abnormal tissue and can be benign (not cancer) or malignant (cancer). A polyp is a benign, non-cancerous tumor. Some polyps can change into cancer, but not all do. The chance of changing into a cancer depends upon the kind of polyp.
Colon Polyps

• **Adenomatous polyps (adenomas)** are polyps that have the potential to change into cancer. Because of this, adenomas are called a pre-cancerous condition.

• **Hyperplastic polyps and inflammatory polyps**, in general, are not pre-cancerous. But some doctors think that some hyperplastic polyps can become pre-cancerous or might be a sign of having a greater risk of developing adenomas and cancer, particularly when these polyps grow in the ascending colon.
Another kind of pre-cancerous condition is called *dysplasia*. Dysplasia is an area in the lining of the colon or rectum where the cells look abnormal (but not like true cancer cells) when seen under a microscope. These cells can change into cancer over time. Dysplasia is usually seen in people who have had diseases such as ulcerative colitis or Crohn’s disease for many years. Both ulcerative colitis and Crohn’s disease cause chronic inflammation of the colon.
Colon cancer facts

- Colorectal cancer is a malignant tumor arising from the inner wall of the large intestine.
- Colorectal cancer is the third leading cause of cancer in males and fourth in females in the U.S.
Colon cancer facts

- Risk factors for colorectal cancer include a family history of colorectal cancer, colon polyps, and long-standing ulcerative colitis.
- Most colorectal cancers develop from polyps. Removal of colon polyps can prevent colorectal cancer.
A diet that is high in red meats (such as beef, pork, lamb, or liver) and processed meats (hot dogs and some luncheon meats) can increase colorectal cancer risk. Cooking meat at very high temperatures (frying, broiling, or grilling) creates chemicals that might increase cancer risk, although it’s not clear how much this might contribute to an increase in colorectal cancer risk. Diets high in vegetables, fruits, and whole grains have been linked with a decreased risk of colorectal cancer, but fiber supplements do not seem to help. Whether other dietary components (like certain types of fats) affect colorectal cancer risk is not clear.
Physical inactivity

• If you are not physically active, you have a greater chance of developing colorectal cancer. Increasing activity may help reduce your risk.
Obesity

• If you are very overweight, your risk of developing and dying from colorectal cancer is increased. Obesity raises the risk of colon cancer in both men and women, but the link seems to be stronger in men.
Long-term smokers are more likely than non-smokers to develop and die from colorectal cancer. Smoking is a well-known cause of lung cancer, but it is also linked to other cancers, like colorectal.
Heavy alcohol use

- Colorectal cancer has been linked to the heavy use of alcohol. Limiting alcohol use to no more than 2 drinks a day for men and 1 drink a day for women could have many health benefits, including a lower risk of colorectal cancer.
Other risk factors

• Age

• Younger adults can develop colorectal cancer, but the chances increase markedly after age 50; about 9 out of 10 people diagnosed with colorectal cancer are at least 50 years old.
Personal history of inflammatory bowel disease

- Inflammatory bowel disease (IBD), which includes ulcerative colitis and Crohn’s disease, is a condition in which the colon is inflamed over a long period of time. People who have had IBD for many years often develop dysplasia. Dysplasia is a term used to describe cells in the lining of the colon or rectum that look abnormal (but not like true cancer cells) when seen under a microscope. These cells can change into cancer over time.

- Inflammatory bowel disease is different from irritable bowel syndrome (IBS), which does not carry an increased risk for colorectal cancer.
Colon cancer facts

• Colon polyps and early cancer may have no symptoms. Therefore regular screening is important.

• Diagnosis of colorectal cancer can be made by barium enema or by colonoscopy with biopsy confirmation of cancer tissue
Colon cancer facts

• Treatment of colorectal cancer depends on the location, size, and extent of cancer spread, as well as the health of the patient.

• Surgery is the most common treatment for colorectal cancer.
Colon cancer facts

- Chemotherapy can extend life and improve quality of life for those who have had or are living with colorectal cancer
The colon has 4 sections

- **Ascending colon.** It starts with a small pouch (the cecum) where the small bowel attaches to the colon and extends upward on the right side of the abdomen. The cecum is also where the appendix attaches to the colon.
- **Transverse colon.** Goes across the body from the right to the left side in the upper abdomen.
- **Descending colon,** continues downward on the left side.
- **Sigmoid colon.** Has a “S” or “sigmoid” shape.
Inherited syndromes

• About 5% to 10% of people who develop colorectal cancer have inherited gene defects (mutations) that can cause family cancer syndromes and lead to them getting the disease. These syndromes often lead to cancer that occurs at a younger age than is usual. They are also linked to other cancers besides colorectal cancer. Some of these syndromes are also linked to polyps.

• The 2 most common inherited syndromes linked with colorectal cancers are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC), but other rarer syndromes can also increase colorectal cancer risk.
Hereditary non-polyposis colon cancer (HNPCC)

- HNPCC, also known as Lynch syndrome, accounts for about 2% to 4% of all colorectal cancers. In most cases, this disorder is caused by an inherited defect in either the gene MLH1 or the gene MSH2, but other genes can also cause HNPCC. Most of the genes involved normally help repair DNA damage.

- The cancers in this syndrome also develop when people are relatively young. People with HNPCC can have polyps, but they only have a few, not hundreds as in FAP. The lifetime risk of colorectal cancer in people with this condition may be as high as 80%.

- Women with this condition also have a very high risk of developing cancer of the endometrium. Other cancers linked with HNPCC include cancer of the ovary, stomach, small bowel, pancreas, kidney, brain, ureters, and bile duct.
Turcot syndrome

• This is a rare inherited condition in which people are at increased risk of adenomatous polyps and colorectal cancer, as well as brain tumors. There are actually 2 types of Turcot syndrome:
  • One can be caused by gene changes similar to those seen in FAP, in which cases the brain tumors are medulloblastomas.
  • The other can also be caused by gene changes similar to those seen in HNPCC, in which cases the brain tumors are glioblastomas.
Peutz-Jeghers syndrome:

- People with this rare inherited condition tend to have freckles around the mouth (and sometimes on their hands and feet) and a special type of polyp (called hamartoma) in their digestive tracts. They are at a greatly increased risk for colorectal cancer, as well as several other cancers, which usually appear at a younger age than usual. This syndrome is caused by mutations in the gene STK11.
MUTYH-associated polyposis:

People with this syndrome develop colon polyps which will become cancerous if the colon is not removed. They also have an increased risk of cancers of the small intestine, skin, ovary, and bladder. This syndrome is caused by mutations in the gene MUTYH.
At Risk

• African Americans have the highest colorectal cancer incidence and mortality rates of all racial groups in the United States. The reasons for this are not yet understood.

• Jews of Eastern European descent (Ashkenazi Jews) have one of the highest colorectal cancer risks of any ethnic group in the world. Several gene mutations leading to an increased risk of colorectal cancer have been found in this group. The most common of these DNA changes, called the *I1307K APC mutation*, is present in about 6% of American Jews.
Type 2 diabetes

- People with type 2 (usually non-insulin dependent) diabetes have an increased risk of developing colorectal cancer. Both type 2 diabetes and colorectal cancer share some of the same risk factors (such as excess weight). But even after taking these factors into account, people with type 2 diabetes still have an increased risk. They also tend to have a less favorable prognosis (outlook) after diagnosis.
Microsatellite instability (MSI)

MSI is the condition of genetic hypermutability that results from impaired DNA mismatch repair (MMR). The presence of MSI represents phenotypic evidence that MMR is not functioning normally.

- MMR corrects errors that spontaneously occur during DNA replication, such as single base mismatches or short insertions and deletions. The proteins involved in MMR correct polymerase errors by forming a complex that binds to the mismatched section of DNA, excises the error, and inserts the correct sequence in its place. Cells with abnormally functioning MMR are unable to correct errors that occur during DNA replication and consequently accumulate errors. This causes the creation of novel microsatellite fragments. Polymerase chain reaction-based assays can reveal these novel microsatellites and provide evidence for the presence of MSI.
Reasons to test for MSI

- The person is younger than 50 years.
- The person has or had a second colorectal cancer or another cancer (endometrial, stomach, pancreas, small intestine, ovary, kidney, brain, ureters, or bile duct) that is associated with HNPCC.
- The person is younger than 60 years and the cancer has certain characteristics seen with HNPCC when viewed under the microscope or with other lab tests.
- The person has a first-degree relative younger than 50 who was diagnosed with colorectal cancer or another cancer often seen in HNPCC carriers (endometrial, stomach, pancreas, small intestine, ovary, kidney, brain, ureters, or bile duct).
- The person has 2 or more first- or second-degree relatives who had colorectal cancer or another HNPCC-related cancer at any age (second-degree relatives include uncles, aunts, grandparents, nieces, nephews and grandchildren).
Microsatellite instability (MSI) and/or immunohistochemistry (IHC) testing is performed to analyze colon and other tumor tissue samples for features suggestive of Lynch syndrome/hereditary non-polyposis colorectal cancer (HNPCC). The tests aid in targeting gene sequencing of the mismatch repair genes (MLH1, MSH2, PMS2 and MSH6) and screen out individuals who are unlikely to have Lynch syndrome. MSI and/or IHC testing are often the first steps for individuals suspected to have Lynch/HNPCC
Basic concepts in the interpretation of MSI and IHC

- MSI testing will identify tumors that have microsatellite instability (i.e., MSI-high tumors)
- IHC testing will detect the presence or absence of the protein products of the mismatch repair genes (MLH1, MSH2, PMS2 and MSH6)
- The odds of having Lynch syndrome in a patient with CRC are approximately one in five if the patient’s tumor is found to be MSI-high or to have abnormal IHC

As a result, MSI and IHC are effective tools to screen for colorectal cancer patients who are more likely to have Lynch syndrome.

When interpreting MSI or IHC results, also consider that:

- Approximately 3 percent of all CRC cases are caused by Lynch syndrome
- About 13 percent of all colorectal tumors are MSI-high
- Approximately 25 percent of all colorectal tumors have abnormal IHC

Thus, MSI and IHC testing are not diagnostic because many patients with MSI-high tumors or tumors with abnormal IHC do not have Lynch syndrome.
Colorectal cancer screening tests

• Flexible sigmoidoscopy

• During this test, the doctor looks at part of the colon and rectum with a sigmoidoscope – a flexible, lighted tube about the thickness of a finger with a small video camera on the end. It is inserted through the rectum and into the lower part of the colon. Images from the scope are viewed on a display monitor.
Colonoscopy

For this test, the doctor looks at the entire length of the colon and rectum with a colonoscope, a thin, flexible, lighted tube with a small video camera on the end. It is basically a longer version of a sigmoidoscope. It is inserted through the anus and into the rectum and colon. Special instruments can be passed through the colonoscope to biopsy or remove any suspicious-looking areas such as polyps, if needed.
The double-contrast barium enema (DCBE) is also called an *air-contrast barium enema* or a *barium enema with air contrast*. It may also be referred to as a *lower GI series*. It is basically a type of x-ray test. Barium sulfate, which is a chalky liquid, and air are used to outline the inner part of the colon and rectum to look for abnormal areas on x-rays. If suspicious areas are seen on this test, a colonoscopy will be needed to explore them further.
CT colonography (virtual colonoscopy)

- This test is an advanced type of computed tomography (CT or CAT) scan of the colon and rectum. A CT scan is an x-ray test that produces detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into images of slices of the part of your body being studied.
Guaiac-based fecal occult blood test

• One way to find for colorectal cancer is to look for blood that can't be seen with the naked eye (occult blood) in feces (stool). The idea behind this test is that blood vessels at the surface of larger colorectal polyps or cancers are often fragile and easily damaged by the passage of feces. The damaged vessels usually release a small amount of blood into the feces, but only rarely is there enough bleeding for blood to be visible in the stool.
Fecal immunochemical test

- The fecal immunochemical test (FIT), also called an *immunochemical fecal occult blood test* (iFOBT), tests for occult (hidden) blood in the stool in a different way than a guaiac-based test. This test reacts to part of the human hemoglobin protein, which is found in red blood cells.
A stool DNA test looks for certain abnormal sections of DNA (genetic material) from cancer or polyp cells. Colorectal cancer cells often contain DNA mutations (changes) in certain genes. Cells from colorectal cancers or polyps with these mutations are often shed into the stool, where tests may be able to detect them. Cologuard™, the test currently available, also tests for blood in the stool.
Hmei-4318

Tumor

Normal colon
Hmei-4138 negative margin 1a

Normal Colon

muscle
Hmei-3197

1b negative margin
Layers of GI tract

Submucosal plexus (Meissner’s plexus)

Glands in submucosa

Vein

Submucosa

Gland in mucosa

Duct of gland outside tract

Lymphatic tissue

Lumen

Mucosa:
   - Epithelium
   - Lamina propria
   - Muscularis mucosae

Muscularis:
   - Circular muscle
   - Longitudinal muscle

Serosa:
   - Areolar connective tissue
   - Epithelium

Layers of the Colon and Rectum

mucosa
submucosa
muscularis propria
serosa

*serosa is not found on most of the rectum
Hmei-4138
1c positive invading muscularis
Hmei-4138
1d positive invading muscularis
Hmei-4138
1e tumor invading muscularis
Hmei-4138

1f tumor invading through muscularis
Hmei-4138
1g negative lymph node
Hmei-4138
1h negative lymph node
Hmei04138
r1i negative lymph node
Hbwi-10632

Distal Surgical Margin 1a
Hbwi-10632
Hbwi-10632
Hbwi-10632
1a distal margin involved with tumor
Hbwi-10632
1b proximal margin negative

Normal Colon
Hbwi-10632
1c mod diff adeno CA

Tumor
Hbwi-10632
1d mod diff adeno CA
Hbwi-10632
1e mod diff adeno CA
Hbwi-10632
1f mod diff adeno CA
Hbwi-10632
1g mod diff adeno CA
Hbwi-10632
1h neg lymph node
Hbwi-10632
1i neg lymph node
Hbwi-10632
1j neg lymph node
Hbwi-10632
1k neg colon
Hbwi-10632
1L neg surg margin
Hbwi-10632
2a benign prox ring
Hbwi-10632
3a benign distal ring
Hbwi-10632
f4a fs neg node
MLH-1
Preserved
MSH-2
Preserved
MSH-6
Preserved
PMS-2 preserved
CPT Codes

• 88309  colon, total resection
• 88342  IHC initial single antibody stain
The End